

WHAT IS CLAIMED:

1. A transgenic non-human animal whose somatic cells and germ cells are homozygous for an altered agouti-related protein (AgRP) gene which encodes a non-functional AgRP protein.
2. The transgenic animal of claim 1 wherein the animal is a mouse whose somatic cells and germ cells are homozygous for an altered agouti-related protein (AgRP) gene which encodes a non-functional AgRP protein, and further wherein said mouse exhibits reduced daytime respiratory quotient.
3. A cell line derived from a transgenic animal of claim 2.
4. A transgenic mouse whose somatic cells are heterozygous for a functional murine gene coding for an agouti-related protein (AgRP) protein and an altered AgRP gene.
5. A cell line derived from a transgenic animal according to Claim 4.
6. A transgenic mouse whose somatic cells are hemizygous for an altered AgRP gene.
7. A cell line derived from a transgenic animal according to Claim 6.
8. A transgenic mouse whose somatic cells and germ cells lack a functional gene coding for a murine agouti-related protein (AgRP) and which contain and express a transgene comprising a gene for a non-native AgRP protein, wherein said mouse is viable.

9. The transgenic mouse of claim 8 wherein said transgene encodes wild-type or a mutant form of human AgRP.

5 10. A method of producing a mouse having somatic and germ cells that lack a murine gene coding for AgRP, which comprises:

- (a) providing a gene encoding an altered form of AgRP designed to target an AgRP allele of mouse embryonic stem cells;
- (b) introducing the altered gene into mouse embryonic stem cells;
- 10 (c) selecting embryonic stem cells which contain the altered gene;
- (d) introducing the embryonic stem cells containing the altered gene into mouse blastocysts;
- (e) transplanting the injected blastocysts into a pseudopregnant mouse, and
- 15 (f) allowing the embryo to develop to term; to produce a chimeric founder transgenic mouse.

11. A transgenic non-human animal whose somatic cells and germ cells are homozygous for an altered agouti-related protein (AgRP) gene which 20 encodes a non-functional AgRP protein and homozygous for an altered Neuropeptide Y (NPY) gene which encodes a non-functional NPY protein.

12. A cell line derived from a transgenic animal of claim 11.

25 13. A transgenic mouse whose somatic cells and germ cells are homozygous for an altered agouti-related protein (AgRP) gene, which encodes a non-functional AgRP protein and homozygous for an altered Neuropeptide Y (NPY) gene which encodes a non-functional NPY protein.

14. A cell line derived from a transgenic mouse of claim 13.

15. A transgenic mouse whose somatic cells are heterozygous or homozygous for an altered AgRP gene and an altered NPY gene, wherein the altered gene encodes a non-functional NPY protein.

5 16. A cell line derived from a transgenic animal according to
Claim 15.

10 17. A transgenic mouse whose somatic cells and germ cells lack a functional genes coding for a murine AgRP protein and a NPY protein which contains and expresses a first transgene encoding a non-native AgRP protein and a second transgene encoding a non-native NPY protein.

15 18. The transgenic mouse of claim 17 wherein said first transgene encodes wild-type human AgRP and said second transgene encodes wild-type human NPY.

19. A method of evaluating the effect of a candidate compound on the expenditure and/or utilization of energy, which comprises:

20 (a) administering the candidate compound to a transgenic mouse in accordance with claim 2; and
(b) measuring the effect of the candidate compound on the expenditure and/or utilization of energy.

25 20. A method of evaluating the effect of a candidate compound on the expenditure and/or utilization of energy, which comprises:

(a) administering the candidate compound to a transgenic mouse in accordance with claim 13; and
(b) measuring the effect of the candidate compound on the expenditure and/or utilization of energy.